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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,243	07/16/2001	Alexander H. Taylor	P50770X1C1	4165

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EXAMINER

HELMS, LARRY RONALD

ART UNIT	PAPER NUMBER
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1642

DATE MAILED: 02/12/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/905,243

Applicant(s)

TAYLOR, ALEXANDER H.

Examiner

Larry R. Helms

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 17 November 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 40-44, 48-62 and 64 is/are pending in the application.
- 4a) Of the above claim(s) 54-59 and 64 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 40-44, 48 and 51 is/are rejected.
- 7) ☐ Claim(s) 49, 50, 52, 53 and 60-62 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
* See the attached detailed Office action for a list of the certified copies not received.
- 13) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.
a) ☐ The translation of the foreign language provisional application has been received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

DETAILED ACTION

1. Claims 1-39 have been canceled.

Claims 45-47, 63 have been canceled.

The second original claim number 46 has been amended to claim 47 and original claims 47-63 have been amended to claims 48-64. The rejections below are for the newly amended claim numbers and the issues/rejections do not change due to the renumbering.

Claim 40 has been amended.

2. Claims 40-44, 48-53 and 60-62 are under examination and will be examined to the extent the species of Pan troglodytes is the elected species of Old World apes.

3. Claims 54-59 and 64 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

4. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.

5. The following Office Action contains NEW GROUNDS of rejection.

Rejections Withdrawn

6. The rejection of claim 46 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.

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7. The rejection of claims 40-47, 50, and 62 under 35 U.S.C. 103(a) as being unpatentable over Adair et al (WO 91/09967, published 7/91, PTO-892, paper #6) and further in view of Vijn-Warrier et al (Molecular Immunology 32:1081-92, 1995, PTO-892, paper #6) is withdrawn in view of the amendments to the claims.

The following are NEW GROUNDS of rejections

Claim Rejections - 35 USC § 103

8. Claims 40-44, 48, 51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Adair et al (WO 91/09967, published 7/91, PTO-892, paper #6) and further in view of Vijn-Warrier et al (Molecular Immunology 32:1081-92, 1995, PTO-892, paper #6) and Queen et al (US Patent 5,693,762, with priority to at least 1990).

The claims recite a variable region comprising CDRs from a rodent and framework regions from Pan troglodytes wherein at least one CDR-contacting amino acid from the acceptor framework is replaced with a donor wherein the CDR-contacting residues contacts a CDR within the van der Waals radius of an antibody or a salt bridge or a hydrophobic interaction and at least one human constant region.

Adair et al teach methods of CDR grafting comprising acceptor framework and donor antigen binding regions of rodent antibodies (see abstract). Adair et al also teach non-CDR framework residues which contribute to antigen binding and CDR contacting residues (see pages 20-23) and replacing residues that influence CDR or antigen binding and those that are in a salt bridge (see page 21) and constant regions from humans (see page 12). Adair et al does not teach that the framework residues be from

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Pan troglodytes or replacing residues within van der Waals radius or hydrophobic interactions. This deficiency is made up for in the teachings of Vijn-Warrier and Queen et al.

Vijn-Warrier et al teach the nucleotide and amino acid sequence of the variable region of a Pan troglodytes antibody (see abstract). Vijn-Warrier also teach several human germline variable region genes (see Figure 3, 4, and 5, and Table 1) and that chimpanzee mAbs are no more likely to elicit deleterious anti-immunoglobulin responses in humans than human mAbs (see page 1089).

Queen et al teach CDR grafting of donor CDRs onto human or humanized frameworks and replacing frameworks of the acceptor when within 3Å or residues influencing the van der Waal forces of a CDR residue or interacting in hydrophobic interactions with a CDR residue (see column 14, lines 26-50).

It would have been prima facie obvious to one of ordinary skill in the art at the time the claimed invention was made to have produced an antibody comprising donor CDRs from a rodent species and acceptor framework residues from Pan troglodytes in view of Adair et al, Vijn-warrier et al and Queen et al.

One of ordinary skill in the art would have been motivated to and have a reasonable expectation of success to produce the claimed invention because Vijn-Warrier et al teach "these findings suggest that chimpanzee mAbs are no more likely to elicit deleterious anti-immunoglobulin responses in humans than are human mAbs" (see page 1089) and that the chimpanzee VH and Vk genes are no more divergent than the human genes. In addition, one of ordinary skill in the art would have been motivated to

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produce the claimed invention because Adair et al teach donor CDRs from non-human species such as rodents (see abstract and page 8, lines 3-7) and Adair et al teach a method comprising retaining residues that are involved with antigen binding or contacting the CDRs or replacing solvent exposed framework residues (see pages 20-23, 38-39, and Figure 3). Moreover, one of ordinary skill in the art would have been motivated to and have a reasonable expectation of success to produce the claimed invention because Queen et al teach CDR grafting and replacing acceptor residues with donor residues when the residue influences CDR presentation, antigen binding and the residues are within van der Waals distance or result in hydrophobic interactions. Thus, it would have been prima facie obvious to have used the framework regions from a Pan troglodyte to produce the claimed antibody due to the high homology between human and Pan troglodytes immunoglobulin amino acid sequences and combine the teachings of Adair and Queen et al who has produced antibodies with rodent CDRs and combine this with chimpanzee frameworks due to the high homology between chimpanzee mAbs and human mAbs as taught by Vijn-Warrier et al. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

The response filed 11/17/03 has been carefully considered but is deemed not to be persuasive. The response states that Neither Adair or Vijn-Warrier et al teach substitution based on acceptor residues within van der Waals radius or salt bridge or hydrophobic interaction and neither suggests human constant regions (see page 8 of response). In response to this argument, Queen et al specifically teach constant

regions of humans and replacing residues that are within van der Waals radius or salt bridge or hydrophobic interaction.

The response further states that Vijn-Warrier et al does not teach a chimeric antibody with CDRs from a rodent and FR from Old World Ape and a human constant region (see page 9 of response). In response to this argument, the response seems to argue the reference separately whereas the rejection is based on a combination of references. Vijn-Warrier et al clearly teach the similarities of human and chimpanzee antibodies and that chimpanzee antibodies would not be anymore immunogenic than human mAbs. Thus it would be obvious that the frameworks that comprise the antigenic regions of the antibody or at least the majority would be replaced in a rodent as taught by Adair et al or Queen to reduce the immunogenicity in a human with chimpanzee frameworks which as taught by Vijn-Warrier et al are almost identical to human frameworks and still low in immunogenicity.

Conclusions

9. No Claims are allowed. Claims 49-50, 52-53, 60-62 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

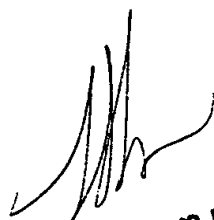
11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (703) 306-5879. The examiner can normally be reached on Monday through Friday from 7:00 am to 4:30 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, can be reached on (703) 308-3559. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 308-4242.

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Respectfully,
Larry R. Helms Ph.D.
703-306-5879



LARRY R. HELMS, PH.D
PRIMARY EXAMINER